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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	: Lindberg et al.
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INFORMATION DISCLSOURE STATEMENT
WITHIN THREE MONTHS OF FILING OR
BEFORE MAILING OF FIRST OFFICE ACTION (37 C.F.R. §1.97(b))

Sir:

Applicants submit this communication in compliance with 37 C.F.R. §§1.56, 1.97 and 1.98.

As disclosed on page 11, lines 6-11 of the subject application, the processes used to obtain the optically pure sodium salt of the (-)-enantiomer of omeprazole result in a change of direction from the (-) to the (+) optical rotation when prepared from the neutral form of the (-)-enantiomer of omeprazole. Thus, the optical rotation of the neutral form of the (-)-enantiomer of omeprazole has a negative direction (See, Example 12, Preparation of (-)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]-sulfinyl]-1H-benzimidazole: $[\alpha]_D^{20}$ -155° (c=0.5%, chloroform)), whereas the sodium salt of the (-)-enantiomer has a positive direction (See, Example 1, Preparation of (+)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]-sulfinyl]-1H-benzimidazole sodium salt: $[\alpha]_D^{20}$ +42.8° (c=0.5%, water)).

Similarly, the process used to obtain the optically pure magnesium salt of the (-)-enantiomer of omeprazole results in a change of direction from the (+) to the (-) optical rotation when prepared from the sodium salt of the (-)-enantiomer. Thus, the rotation of the magnesium salt of the (-)-enantiomer of omeprazole has a negative direction (See, Example 5, Preparation of (-)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]-sulfinyl]-1H-benzimidazole magnesium salt: $[\alpha]_D^{20}$ -128.2° (c=1%, methanol).

This phenomenon is also reported by Sverker von Unge et al., "Stereochemical assignment of the enantiomers of omeprazole from X-ray analysis of a fenchyloxymethyl derivative of (+)-(R)-omeprazole", Tetrahedron: Asymmetry, Vol. 8, No. 12, pp. 1967-1970, 1997. Specifically, von Unge et al. disclose that the sign of the optical rotation is reversed in relation to that of the neutral form when the measurement of the optical rotation is performed with the enantiomers of omeprazole as sodium salts dissolved in water. Thus, the R-enantiomer as the sodium salt has the optical rotation $[\alpha]_D^{20}$ -44.1° (c=0.5%, water), whereas the R-enantiomer in neutral form has the optical rotation $[\alpha]_D^{20}$ +181.5° (c=0.5%, chloroform).

Notwithstanding the change in optical rotation as discussed, the absolute configuration of the compound remains the same.

The von Unge et al. publication and U.S. Patent No. 5,888,535 are listed on the PTO-1449 and a copy of both is enclosed.

TIME OF TRANSMITTAL OF INFORMATION DISCLSOURE STATEMENT

The information disclosure statement transmitted herewith is being filed within three months of the filing date of the application or date of entry into the national stage of an international application or before the mailing date of a first Office action on the merits, whichever event occurs last.

Applicants submit that no fee is required in connection with this submission. However, if any fee or additional fees are due in connection with the communication, authorization is hereby given to charge Account No. 23-1703.

Dated: November 12, 1999

Respectfully submitted,

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Enclosures

Form PTO-1149

Sverker von Unge et al., "Stereochemical assignment of the enantiomers of omeprazole from X-ray analysis of a fenchyloxymethyl derivative of (+)-(R)-omeprazole, Tetrahedron: Asymmetry, Vol. 8, No. 12, pp. 1967-1970, 1997

U.S. Patent No. 5,888,535